

PTO/SB/21 (09-04)

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**TRANSMITTAL  
FORM**

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

12

Application Number

10/540,808

Filing Date

December 23, 2003

First Named Inventor

Marco Muda

Art Unit

Not yet assigned

Examiner Name

Not yet assigned

Attorney Docket Number

05558.0029.PCUS00

**ENCLOSURES (Check all that apply)**☐ Fee Transmittal Form☐ Fee Attached☐ Amendment/Reply☐ After Final☐ Affidavits/declaration(s)☐ Extension of Time Request☐ Express Abandonment Request☒ Information Disclosure Statement☐ Certified Copy of Priority Document(s)☐ Response to Missing Parts/  
Incomplete Application☐ Response to Missing Parts  
under 37 CFR 1.52 or 1.53☐ Drawing(s)☐ Licensing-related Papers☐ Petition☐ Petition to Convert to a  
Provisional Application☐ Power of Attorney, Revocation  
Change of Correspondence Address☐ Terminal Disclaimer☐ Request for Refund☐ CD, Number of CD(s) \_\_\_\_\_☐ Landscape Table on CD☐ After Allowance Communication to TC☐ Appeal Communication to Board  
of Appeals and Interferences☐ Appeal Communication to TC  
(Appeal Notice, Brief, Reply Brief)☐ Proprietary Information☐ Status Letter☒ Other Enclosure(s) (please identify  
below):PTO/SB/08A & PTO/SB08B;  
cited references; and postcard

Remarks

**SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT**

Firm Name

Howrey LLP

Signature

Printed name

David W. Clough, Ph.D.

Date

April 6, 2006

Reg. No.

36,107

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Marco Muda  
App. No.: 10/540,808  
Filing Date: December 23, 2003  
Attorney Docket No. 05558.0029.PCUS00  
Conf. No.: 1050  
Title: SPLICED VARIANTS OF LGR6

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David W. Clough, Ph.D.

Registration No. 36207

**INFORMATION DISCLOSURE STATEMENT  
PURSUANT TO 37 C.F.R. §§ 1.56, 1.97 and 1.98**

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In compliance with 37 C.F.R. § 1.97 and the continuing duty of disclosure under 37 C.F.R. § 1.56, Applicants call to the attention of the Examiner the references listed on the attached Forms PTO/SB/08A and PTO/SB/08B. It is respectfully requested that this Information Disclosure Statement be entered and the documents listed on attached Forms PTO/SB/08A and PTO/SB/08B be considered by the Examiner and made of record.

In accordance with 37 C.F.R. § 1.97(g), this Information Disclosure Statement is not to be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), this Information Disclosure Statement is not to be construed as an admission that the information cited is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

This Information Disclosure Statement does not include copies of cited U.S. patents and U.S. patent publications pursuant to 37 C.F.R. 1.98(a)(2).

This Information Disclosure Statement is being filed prior to the receipt of a first Office Action reflecting an examination on the merits, and hence is believed to be timely filed in accordance with 37 C.F.R. § 1.97(b)(3).

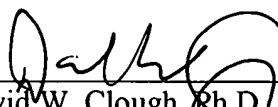
No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to this document, the Commissioner is hereby authorized to deduct the fees from Howrey Simon Arnold & White, LLP Deposit Account 08-3038 referencing docket number 05558.0029.PCUS00.

Respectfully submitted,

HOWREY LLP

Dated: April 6, 2006

By: \_\_\_\_\_

  
David W. Clough, Ph.D.

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PTO/SB/08A (08-03)

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Substitute for form 1449/PTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

### Complete if Known

Application Number	10/540,808
Filing Date	December 23, 2003
First Named Inventor	Marco Muda
Group Art Unit	
Examiner Name	
Attorney Docket Number	05558.0029.PCUS00

Sheet 1 of 2

### U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number - Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	3,773,919	11/20/1973	Boswell, et al.	
	A8	4,816,567	03/28/1989	Cabilly, et al.	
	A3	5,272,071	12/21/1993	Chappel	
	A4	5,585,089	12/17/1996	Queen, et al.	
	A5	5,693,762	12/02/1997	Queen, et al.	
	A6	5,723,323	03/03/1998	Kauffman, et al.	
	A7	5,763,192	06/09/1998	Kauffman, et al.	
	A8	5,814,476	09/29/1998	Kauffman, et al.	
	A9	5,817,483	10/06/1998	Kauffman, et al.	
	A10	5,824,469	10/20/1998	Horwitz, et al.	

### FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
	B1	EP 0 036 676	09/30/1981	The Regents of the University of California		
	B2	EP 0 058 481	08/25/1982	Imperial Chemical Industries PLC		
	B3	EP 0 088 046	09/07/1983	CIBA-Geigy AG		
	B4	EP 0 133 988	03/13/1985	Hoechst Aktiengesellschaft		
	B5	EP 0 143 949	06/12/1985	Nakagame, Fujio		
	B6	WO 01/85768 A2	11/15/2001	Millennium Pharmacaaceuticals, Inc.		
	B7	WO 02/06851 A1	01/24/2002	Robert Bosch GMBH		
	B8	WO 02/29038 A2	04/11/2002	Curagen Corporation		
	B9	WO 91/09955	07/11/1991	Applied Research Systems, ARS Holding M.V.		
	B10	WO 94/20069	09/15/1994	Amgen Inc.		
	B11	WO 99/15545	04/01/1999	Merck & Co., Inc.		

Examiner  
Signature

Date  
Considered

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				<b>First Named Inventor</b>	Marco Muda
				<b>Group Art Unit</b>	
				<b>Examiner Name</b>	
Sheet	2	of	2	<b>Attorney Docket Number</b>	05558.0029.PCUS00

[illegible]

<b>Examiner Signature</b>		<b>Date Considered</b>	
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				<b>Examiner Name</b>	
Sheet	1	of	7	<b>Attorney Docket Number</b>	05558.0029.PCUS00

<b>NON PATENT LITERATURE DOCUMENTS</b>			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T <sup>2</sup>
	C1	Adams, J., et al., "The c-myc Oncogene Driven by Immunoglobulin Enhancers Induces Lymphoid Malignancy in Transgenic Mice," Nature, Vol. 318, No. 12, pp. 533-538 (1985)	
	C2	Alexander, W., "Expression of the c-myc Oncogene under Control of an Immunoglobulin Enhancer in Eμ-myc Transgenic Mice," Molecular and Cellular Biology, Vol. 7, No. 4, pp. 1436-1444 (1987)	
	C3	Benoist, C., et al., "In vivo Sequence Requirements of the SV40 Early Promoter Region," Nature, Vol. 290, pp. 304-310 (1981)	
	C4	Bhowmick, N., et al., "Determination of Residues Important in Hormone Binding to the Extracellular Domain of the Luteinizing Hormone/Chorionic Gonadotropin Receptor by Site-Directed Mutagenesis and Modeling," Molecular Endocrinology, Vol. 10, No. 9, pp. 1147-1159 (1996)	
	C5	Braun, T., "Amino-Terminal Leucine-Rich Repeats in Gonadotropin Receptors Determine Hormone Selectivity," The EMBO Journal, Vol. 10, No. 7, pp. 1885-1890 (1991)	
	C6	Brinster, R., "Regulation of Metallothionein-Thymidine Kinase Fusion Plasmids Injected Into Mouse Eggs," Nature, Vol. 296, pp. 39-42 (1982)	
	C7	Brodeur, B., et al., "Mouse-Human Myeloma Partners for the Production of Heterohybridomas," Chapter 4, pp. 51-63 (1987)	
	C8	Davis, S., et al., "Isolation of Angiopoietin-1, a Ligand for the TIE2 Receptor, by Secretion-Trap Expression Cloning," Cell, Vol. 87, pp. 1161-1169 (1996)	
	C9	De Boer, H., et al., "The tac Promoter: A Functional Hybrid Derived from the trp and lac Promoters," Proc. Natl. Acad. Sci. USA, Vol. 80, pp. 21-25 (1983)	
	C10	Doetschman, T., et al., "Targeted Mutation of the Hprt Gene in Mouse Embryonic Stem Cells," Proc. Natl. Acad. Sci. USA, Vol. 85, pp. 8583-8587 (1988)	

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				<b>Group Art Unit</b>	
<b>Examiner Name</b>					
Sheet	2	of	7	<b>Attorney Docket Number</b>	05558.0029.PCUS00

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	C11	Doetschman, T., et al., "Targetted Correction of a Mutant HPRT Gene In Mouse Embryonic Stem Cells," Nature, Vol. 330, pp. 576-578 (1987)	
	C12	Dufau, M., "The Luteinizing Hormone Receptor," Annu. Rev. of Physiol., Vol. 60, pp. 461-496 (1998)	
	C13	El Tayar, N., "Advances in the Molecular Understanding of Gonadotropins-Receptors Interactions," Molecular and Cellular Endocrinology, Vol. 125, pp. 65-70 (1996)	
	C14	Engels, J., et al., "Gene Synthesis," Angew. Chem. Int. Ed. Engl., Vol. 28, pp. 716-734 (1989)	
	C15	Eppstein, D., et al., "Biological Activity of Liposome-Encapsulated Murine Interferon $\gamma$ is Mediated by a Cell Membrane Receptor," Proc. Natl. Acad. Sci. USA, Vol. 82, pp. 3688-3692 (1985)	
	C16	Grosschedl, R., et al., "Introduction of a $\mu$ Immunoglobulin Gene Into The Mouse Germ Line: Specific Expression in Lymphoid Cells and Synthesis of Functional Antibody," Cell, Vol. 38, pp. 647-658 (1984)	
	C17	Gutkind, J., et al., "The Pathways Connecting G Protein-coupled Receptors to the Nucleus through Divergent Mitogen-Activated Protein Kinase Cascades," The Journal of Biological Chemistry, Vol. 273, No. 4, pp. 1839-1842 (1998)	
	C18	Hammer, R., et al., "Diversity of Alpha-Fetoprotein Gene Expression in Mice is Generated by a Combination of Separate Enhancer Elements," Science, Vol. 235, pp. 53-58 (1987)	
	C19	Hanahan, D., "Heritable Formation of Pancreatic $\beta$ -cell Tumours in Transgenic Mice Expressing Recombinant Insulin/Simian Virus 40 Oncogenes," Nature, Vol. 315, pp. 115-122 (1985)	
	C20	Holtzman, E., et al., "A Null Mutation in the Vasopressin V2 Receptor Gene (AVPR2) Associated with Nephrogenic Diabetes Insipidus in the Hopewell Kindred," Human Molecular Genetics, Vol. 2, No. 8, pp. 1201-1204 (1993)	

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<b>Sheet</b>	3	of	7	<b>Attorney Docket Number</b>	05558.0029.PCUS00

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	C21	Houghten, R., et al., "General Method for the Rapid Solid-Phase Synthesis of Large Numbers of Peptides: Specificity of Antigen-Antibody Interaction at the Level of Individual Amino Acids," Proc. Natl. Acad. Sci. USA, Vol. 82, pp. 5131-5135 (1985)	
	C22	Hsu, S., et al., "Activation of Orphan Receptors by the Hormone Relaxin," Science, Vol. 295, pp. 671-674 (2002)	
	C23	Hsu, S., et al., "Characterization of Two LGR Genes Homologous to Gonadotropin and Thyrotropin Receptors with Extracellular Leucine-Rich Repeats and a G Protein-Coupled, Seven-Transmembrane Region," Molecular Endocrinology, Vol. 12, No. 12, pp. 1830-1845 (1998)	
	C24	Hsu, S., et al., "The Three Subfamilies of Leucine-Rich Repeat-Containing G Protein-Coupled Receptors (LGR): Identification of LGR6 and LGR7 and the Signaling Mechanism for LGR7," Molecular Endocrinology, Vol. 14, No. 8, pp. 1257-1271 (2000)	
	C25	Jones, P., et al., "Replacing the Complementarity-Determining Regions in a Human Antibody with Those from a Mouse," Nature, Vol. 321, pp. 522-525 (1986)	
	C26	Kelsey, G., et al., "Species- and Tissue-Specific Expression of Human $\alpha_1$ -Antitrypsin in Transgenic Mice," Genes & Development, Vol. 1, pp. 161-171 (1987)	
	C27	Kitts, P., et al., "A Method for Producing Recombinant Baculovirus Expression Vectors at High Frequency," Biotechniques, Vol. 14, No. 5, pp. 810-817 (1993)	
	C28	Kohler, G., et al., "Continuous Cultures of Fused Cells Secreting Antibody of Predefined Specificity," Nature, Vol. 256, pp. 495-497 (1975)	
	C29	Kollias, G., et al., "Regulated Expression of Human $\gamma$ -, $\beta$ -, and Hybrid $\gamma\beta$ -Globin Genes in Transgenic Mice: Manipulation of the Developmental Expression Patterns," Cell, Vol. 46, pp. 89-94 (1986)	

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	C30	Kozbor, D., et al., "A Human Hybrid Myeloma for Production of Human Monoclonal Antibodies," The Journal of Immunology, Vol. 133, No. 6, pp. 3001-3005 (1984)	
	C31	Kucherlapati, R., "Homologous Recombination in Mammalian Somatic Cells," Progress in Nuclear Acid Research and Molecular Biology, Vol. 36, pp. 301-310 (1989)	
	C32	Krumlauf, R., "Developmental Regulation of $\alpha$ -Fetoprotein Genes in Transgenic Mice", Molecular and Cellular Biology, Vol. 5, No. 7, pp. 1639-1648 (1985)	
	C33	Langer, "Controlled Release of Macromolecules", Chemtech, pp. 98-105 (1982)	
	C34	Langer, R., et al., "Biocompatibility of Polymeric Delivery Systems for Macromolecules," Vol. 15, pp. 267-277 (1981)	
	C35	Lathe, R., "Synthetic Oligonucleotide Probes Deduced from Amino Acid Sequence Data Theoretical and Practical Considerations," Journal of Molecular Biology," Vol. 183, pp. 1-12 (1985)	
	C36	Leder, A., et al., "Consequences of Widespread Deregulation of the c-myc Gene in Transgenic Mice: Multiple Neoplasms and Normal Development," Cell, Vol. 45, pp. 485-495 (1986)	
	C37	Luckow, V., "Baculovirus Systems for the Expression of Human Gene Products," Current Opinion in Biotechnology, Vol. 4, pp. 564-572 (1993)	
	C38	Luckow, V., et al., "Efficient Generation of Infectious Recombinant Baculoviruses by Site-Specific Transposon-Mediated Insertion of Foreign Genes into a Baculovirus Genome Propagated in <i>Escherichia coli</i> ," Journal of Virology, Vol. 67, No. 8, pp. 4566-4579 (1993)	
	C39	Magram, J., et al., "Developmental Regulation of a Cloned Adult $\beta$ -Globin Gene in Transgenic Mice," Nature, Vol. 315, pp. 338-340 (1985)	
	C40	Mason, A., et al., "The Hypogonadal Mouse: Reproductive Functions Restored by Gene Therapy," Science, Vol. 234, pp. 1372-1378 (1986)	

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				<b>Application Number</b>	10/540,808
				<b>Filing Date</b>	December 23, 2003
				<b>First Named Inventor</b>	Marco Muda
				<b>Group Art Unit</b>	
				<b>Examiner Name</b>	
<b>Sheet</b>	5	of	7	<b>Attorney Docket Number</b>	05558.0029.PCUS00

<b>NON PATENT LITERATURE DOCUMENTS</b>			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T <sup>2</sup>
	C41	McDonald, T., et al., "Identification and Cloning of an Orphan G Protein-Coupled Receptor of the Glycoprotein Hormone Receptor Subfamily," Biochemical and Biophysical Research Communications, Vol. 247, pp. 266-270 (1998)	
	C42	McKusick, V., et al., "The Morbid Anatomy of the Human Genome: Chromosomal Location of Mutations Causing Disease," Journal of Med Genetics, Vol. 30, pp. 1-26 (1993)	
	C43	Merrifield, R., "Solid Phase Peptide Synthesis I. The Synthesis of a Tetrapeptide," Journal of the American Chemical Society, Vol. 85, p. 2149-54 (1963)	
	C44	Morrison, S., et al., "Chimeric Human Antibody Molecules: Mouse Antigen-Binding Domains with Human Constant Region Domains," Proc. Natl. Acad. Sci. USA, Vol. 81, pp. 6851-6855 (1984)	
	C45	Nathans, J., et al., "Molecular Genetics of Human Visual Pigments," Annual Review of Genetics, Vol. 26, pp. 403-424 (1992)	
	C46	OMIM, Cadherin-Associated Protein, Beta; CTNNB ( <a href="http://www.ncbi.nlm.nih.gov/entrez/dispomin.cgi?id=116806">http://www.ncbi.nlm.nih.gov/entrez/dispomin.cgi?id=116806</a> )	
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	C49	Pinkert, C., et al., "An Albumin Enhancer Located 10 kb Upstream Functions Along With Its Promoter to Direct Efficient, Liver-Specific Expression in Transgenic Mice," Genes and Development, Vol. 1, pp. 268-276 (1987)	

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	C50	Readhead, C., et al., "Expression of a Myelin Basic Protein Gene in Transgenic Shiverer Mice: Correction of the Dysmyelinating Phenotype," Cell, Vol. 48, pp. 703-712 (1987)	
	C51	Riechmann, L., et al., "Reshaping Human Antibodies for Therapy," Nature, Vol. 332, pp. 323-327 (1998)	
	C52	Roberts, R., "Totally <i>in vitro</i> Protein Selection Using mRNA-Protein Fusions and Ribosome Display," Current Opinion in Chemical Biology, Vol. 3, pp. 268-273 (1999)	
	C53	Roberts, R., et al., "RNA-Peptide Fusions for the <i>in vitro</i> Selection of Peptides and Proteins," Proc. Natl. Acad. Sci. USA, Vol. 94, pp. 12297-12302 (1997)	
	C54	Segaloff, D., et al., "Structure of the Lutropin/Choriogonadotropin Receptor," Recent Progress in Hormone Research, Vol. 46, pp. 261-303 (1990)	
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	C56	Selbie, L., et al., "G Protein-Coupled-Receptor Cross-Talk: The Fine-Tuning of Multiple Receptor-Signalling Pathways," Trends in Pharmacological Sciences, Vol. 19, pp. 87-93 (1998)	
	C57	Shani, M., "Tissue-Specific Expression of Rat Myosin Light-Chain 2 Gene in Transgenic Mice," Nature, Vol. 314, pp. 283-286 (1985)	
	C58	Sidman, K., et al., "Controlled Release of Macromolecules and Pharmaceuticals from Synthetic Polypeptides Based on Glutamic Acid," Biopolymers, Vol. 22, pp. 547-556 (1983)	
	C59	Spiegel, A., et al., "Abnormalities in G Protein-Coupled Signal Transduction Pathways in Human Disease," Journal of Clinical Investigation, Inc., Vol. 92, pp. 1119-1125 (1993)	

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	C60	Strader, C., et al., "Structure and Function of G Protein-Coupled Receptors," Annual Review of Biochemistry, Vol. 63, pp. 101-132 (1994)	
	C61	Swift, G., et al., "Tissue-Specific Expression of the Rat Pancreatic Elastase I Gene in Transgenic Mice," Cell, Vol. 38, pp. 639-656 (1984)	
	C62	Thomas, D., et al. "Mutational Analyses of the Extracellular Domain of the Full-Length Lutropin/Choriogonadotropin Receptor Suggest Leucine-Rich Repeats 1-6 are Involved in Hormone Binding," Molecular Endocrinology, Vol. 10, No. 6, pp. 760-768 (1996)	
	C63	Thomas, K., et al., "High Frequency Targeting of Genes to Specific Sites in the Mammalian Genome" Cell, Vol. 44, pp. 419-428 (1986)	
	C64	Thomas, K., et al., "Site-Directed Mutagenesis by Gene Targeting in Mouse Embryo-Derived Stem Cells," Cell, Vol. 51, pp. 503-512 (1987)	
	C65	Urlaub, G., et al., "Isolation of Chinese Hamster Cell Mutants Deficient in Dihydrofolate Reductase Activity," Proc. Natl. Acad. Sci. USA, Vol. 77, No. 7, pp. 4216-4220, (1980)	
	C66	Verhoeven, M., et al., "Reshaping Human Antibodies: Grafting an Antilysozyme Activity," Science, Vol. 239, pp. 1534-1536 (1988)	
	C67	Villa-Komaroff, L., et al., "A Bacterial Clone Synthesizing Proinsulin," Proc. Natl. Acad. Sci. USA, Vol. 75, No. 8, pp. 3727-3731 (1978)	
	C68	Wagner, M., et al., "Nucleotide Sequence of the Thymidine Kinase Gene of Herpes Simplex Virus Type 1," Proc. Natl. Acad. Sci. USA, Vol. 78, No. 3, pp. 1441-1445 (1981)	
	C69	Yamamoto, T., "Identification of a Functional Promoter in the Long Terminal Repeat of Rous Sarcoma Virus," Cell, Vol. 22, pp. 787-797 (1980)	
	C70	Y. Yamamoto, "Overexpression of Orphan G-Protein-Coupled Receptor, Gpr49, in Human Hepatocellular Carcinomas With $\beta$ -Catenin Mutations	

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